## PATENT COOPERATION TREATY

To:

From the	INTERNATIONAL	BUREAU
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## **PCT**

### **NOTIFICATION OF ELECTION**

(PCT Rule 61.2)

Assistant Commissioner for Patents United States Patent and Trademark Office

Box PCT Washington, D.C.20231

X-12239

**ETATS-UNIS D'AMERIQUE** 

Date of mailing (day/month/year)

in its capacity as elected Office

02 May 2000 (02.05.00)

International application No.

Applicant's or agent's file reference

International filing date (day/month/year)

Priority date (day/month/year)

30 August 1999 (30.08.99) 01 September 1998 (01.09.98)

**Applicant** 

EDMONDS, Brian, Taylor

PCT/US99/19436

	•
1.	The designated Office is hereby notified of its election made:
	X in the demand filed with the International Preliminary Examining Authority on:
	03 March 2000 (03.03.00)
	in a notice effecting later election filed with the International Bureau on:
2.	The election X was
	was not
	made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland

Authorized officer

Pascal Piriou

Telenhone No · 141-221 338 83 38

Faccimile No + (11.22) 740 14 35

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# PATENT COOPERATION TREAT

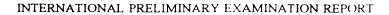
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## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference X-12239	FOR FURTHER ACTION See Not Prelimina	ification of Transmittal of International ry Examination Report (Form PCT/IPEA/416)
International application No.	International filing date (day/month/year)	Priority date (day/month/year)
PCT/US99/19436	30 AUGUST 1999	01 SEPTEMBER 1998
International Patent Classification (IPC) Please See Supplemental Sheet.	) or national classification and IPC	
Applicant ELI LILLY AND COMPANY		
This international prelimit Examining Authority and i     This REPORT consists of a	nary examination report has been preps transmitted to the applicant according a total of sheets.	pared by this International Preliminary to Article 36.
been amended and are (see Rule 70.16 and Se	the basis for this report and/or sheets contain ection 607 of the Administrative Instruction	scription, claims and/or drawings which have sing rectifications made before this Authority. s under the PCT).
These annexes consist of a	total of <u>U</u> sheets.	
3. This report contains indicati	ons relating to the following items.	
I X Basis of the rep	port	
II Priority		
ا ا	ent of report with regard to novelty, inve	entive step or industrial applicability
<u></u>		marke stop of management approaching
IV Lack of unity of		no de la companya de la constanta de la consta
	ient under Article 35(2) with regard to nove planations supporting such statement	elty, inventive step or industrial applicability;
VI Certain documen	ts cited	
VII Certain defects in	the international application	
	ons on the international application	
VIII Certain observad	ons on the international application	
Date of submission of the demand	Date of comple	tion of this report
Date of submission of the demand 03 MARCH 2000	Date of comple	
	21 NOVEM  Authorized office	BER 2000



International application No.

PCT/US99/19436

I. Ba	sis of t	he report		
1. With	regard to	the elements of the internal	tional application:*	
x	-	rnational application as		
		cription:		
X		1-51		as originally filed
		NONE		filed with the demand
		NONE	, filed with the letter of	, filed with the demand
	pages _		, med with the letter of	
$\mathbf{x}$	the clai	ms:		
لت	pages _	52-57		, as originally filed
	pages _		, as amended (together wi	th any statement) under Article 19
	pages _	NONE		, filed with the demand
	pages _	NONE	, filed with the letter of	
X	the drav	MONIO		
	pages			
	pages _		C1 1 11 11 11 11 11 11 11 11 11 11 11 11	
	pages _	NONE	, filed with the letter of	
$\overline{\mathbf{x}}$	the con	nence listing part of the d	esorintion:	
	nie sedi			as originally filed
			W	
	pages _	NONE	, filed with the letter of	, med with the demand
	the lang	guage of a translation fur guage of publication of t	ned to this Authority in the following language mished for the purposes of international some the international application (under Rule 4)	earch (under Rule 23.1(b)). 8.3(b)).
	the languor 55.3).		ished for the purposes of international prelimit	nary examination (under Rules 55.2 and/
			amino acid sequence disclosed in the inter- out on the basis of the sequence listing:	national application, the international
X	containe	ed in the international ap	oplication in printed form.	
			onal application in computer readable form	n.
一			authority in written form.	
一一			authority in computer readable form.	
H	The state	ement that the subsequen	tly furnished written sequence listing does r	not go beyond the disclosure in the
	internati	onal application as filed l	has been furnished.	•
	The state been fun	ement that the information nished.	recorded in computer readable form is identic	al to the writen sequence listing has
4. X	The am	endments have resulted	in the cancellation of:	
	X th	e description, pages	NONE	
		e claims, Nos.	NONE	
		e drawings, sheets/fig		
5.			ome of) the amendments had not been made, s	ince they have been considered to go
			ndicated in the Supplemental Box (Rule 70.2(c	=
in th	icement s	heets which have been furni	shed to the receiving Office in response to an in are not annexed to this report since they do	vitation under Article 14 are referred to
**Any	replacen	nent sheet containing such	amendments must be referred to under item	I and annexed to this report.



International application No. PCT/US99/19436

III. N	III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability			
1. The cindu	questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be strially applicable have not been and will not be examined in respect of:			
	the entire international application.			
X	claims Nos. <u>8, 9, 13, 15-31</u>			
	because:			
	the said international application, or the said claim Nos. relate to the following subject matter which does not require international preliminary examination (specify).			
	the description, claims or drawings (indicate particular elements below) or said claims Nos. are so unclear that no meaningful opinion could be formed (specify).			
	the claims, or said claims Nos _ are so inadequately supported by the description that no meaningful opinion could be formed.			
X	no international search report has been established for said claims Nos. 13, 15-31			
2. A m	neaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid ence listing to comply with the standard provided for in Annex C of the Administrative Instructions:			
	the written form has not been furnished or does not comply with the standard.			
	the computer readable form has not been furnished or does not comply with the standard.			

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US99/19436

v.	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
	citations and explanations supporting such statement

1.	statement			
	Novelty (N)	Claims Claims	1-3, 5-7, 10-12, 14 4	YES NO
	Inventive Step (IS)	Claims Claims	NONE 1-7, 10-12, 14	YES
	Industrial Applicability (IA)	Claims Claims	1-7, 10-12, 14 NONE	YES NO

2. citations and explanations (Rule 70.7)

Claims 1-3, 5-7, 10-12, 14 meet the criteria set out in PCT Article 33(2), because a single prior art reference does not teach or fairly suggest the claimed polypeptides or polynucleotides.

Claims 1-7, 10-12, 14 meet the criteria set out in PCT Article 33(2)and(4), because the claimed polypeptides or polynucleotides have utility in the biotechnology industry.

Claim 4 lacks novelty under PCT Article 33(2) as being anticipated by Database GenBank Accession No. AF011407. Database GenBank Accession No. AF011407 teaches an isolated nucleic acid molecule that hybridizes under stringent conditions to the complement of SEQ ID NO:1.

Claims 1-7, 10-12, 14 lack an inventive step under PCT Article 33(3) as being obvious over YIN in view of Database GenBank Accession No. AAB64201 and Database GenBank Accession No. AF011407. YIN teaches the cloning of a mouse LTBP-3 precursor (page 10149, column 1, full paragraph 1). YIN's mouse LTBP-3 cDNA is 86.5% identical at the nucleotide level to SEQ ID NO: 1 of the instant invention. The predicted polypeptide is 87.5% identical at the amino acid level to SEQ ID NO:2 of the instant invention. YIN also teaches vectors comprising the mouse LTBP-3 cDNA, host cells comprising the vector, a method of producing the encoded polypeptide, and the isolated polypeptide (page 10148, column 2, full paragraphs 3-5; page 10158, Figure 7). YIN also teach isolation of fragments of the human LTBP-3 gene and the coding sequence thereof (paragraph bridging pages 10157-10158). YIN also teaches it will be important to determine if LTBP-3 binds calcium and other molecules (page 10159, full paragraph 2). YIN is silent with respect to the amino acid and nucleotide sequence of the human LTBP-3. However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to clone the human LTBP-3 cDNA with a reasonable expectation of success, using techniques such as those used by LIN for the cloning of the mouse LTBP-3 cDNA. One of ordinary skill in (Continued on Supplemental Sheet.)

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US99/19436

Sup	plem	ental	Box
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(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

#### CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below: IPC(7): C07K 14/47; C07H 21/04; C12N 1/21, 15/00; C12P 21/00 and US C1.: 530/350; 536/23.5; 435/7.1, 69.1, 252.3, 320.1

## V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

kill in the art at the time of Applicants' invention to recombinantly express the encoded human LTBP-3 polypeptide with a easonable expectation of success, using techniques such as those used by LIN for the recombinant expression of the mouse TBP-3 polypeptide. One of ordinary skill in the art would be motivated to express the human LTBP-3 polypeptide ecombinantly because the supply of many eukaryotic proteins which have potential clinical or industrial use is often limited by neir low natural availability; gene cloning and expression in (E. coli, bacteria, yeast, etc.) would provide a more abundant ource of the human LTBP-3 polypeptide. Recombinant expression would provide a convenient source of readily purified rotein. The human LTBP-3 polypeptide comprises at least 20 contiguous amino acids of the instantly disclosed SEQ ID 80:2, as evidenced by Database GenBank Accession No. AAB64201. The human LTBP-3 cDNA can hybridize to the instantly disclosed SEQ ID NO:1, as evidenced by Database GenBank Accession No. AF011407. It would have been obvious one of ordinary skill in the art at the time of Applicants' invention to test for the binding of the human LTBP-3 polypeptide or calcium or other compounds because YIN suggests that importance of doing so.	the art would be motivated to clone the human LTBP-3 cDNA for the recombinant production of the encoded human LTBP-3
easonable expectation of success, using techniques such as those used by LIN for the recombinant expression of the mouse TBP-3 polypeptide. One of ordinary skill in the art would be motivated to express the human LTBP-3 polypeptide ecombinantly because the supply of many eukaryotic proteins which have potential clinical or industrial use is often limited by neir low natural availability; gene cloning and expression in (E. coli, bacteria, yeast, etc.) would provide a more abundant ource of the human LTBP-3 polypeptide. Recombinant expression would provide a convenient source of readily purified rotein. The human LTBP-3 polypeptide comprises at least 20 contiguous amino acids of the instantly disclosed SEQ ID 80:2, as evidenced by Database GenBank Accession No. AAB64201. The human LTBP-3 cDNA can hybridize to the instantly disclosed SEQ ID NO:1, as evidenced by Database GenBank Accession No. AF011407. It would have been obvious of one of ordinary skill in the art at the time of Applicants' invention to test for the binding of the human LTBP-3 polypeptide to calcium or other compounds because YIN suggests that importance of doing so.	polypeptide or analysis of expression of the human LTBP-3 mRNA in tissues. It would have been obvious to one of ordinary
TBP-3 polypeptide. One of ordinary skill in the art would be motivated to express the human LTBP-3 polypeptide ecombinantly because the supply of many eukaryotic proteins which have potential clinical or industrial use is often limited by neir low natural availability; gene cloning and expression in (E. coli, bacteria, yeast, etc.) would provide a more abundant ource of the human LTBP-3 polypeptide. Recombinant expression would provide a convenient source of readily purified rotein. The human LTBP-3 polypeptide comprises at least 20 contiguous amino acids of the instantly disclosed SEQ ID 80:2, as evidenced by Database GenBank Accession No. AAB64201. The human LTBP-3 cDNA can hybridize to the instantly disclosed SEQ ID NO:1, as evidenced by Database GenBank Accession No. AF011407. It would have been obvious of one of ordinary skill in the art at the time of Applicants' invention to test for the binding of the human LTBP-3 polypeptide to calcium or other compounds because YIN suggests that importance of doing so.	skill in the art at the time of Applicants' invention to recombinantly express the encoded human LTBP-3 polypeptide with a
TBP-3 polypeptide. One of ordinary skill in the art would be motivated to express the human LTBP-3 polypeptide ecombinantly because the supply of many eukaryotic proteins which have potential clinical or industrial use is often limited by neir low natural availability; gene cloning and expression in (E. coli, bacteria, yeast, etc.) would provide a more abundant ource of the human LTBP-3 polypeptide. Recombinant expression would provide a convenient source of readily purified rotein. The human LTBP-3 polypeptide comprises at least 20 contiguous amino acids of the instantly disclosed SEQ ID 80:2, as evidenced by Database GenBank Accession No. AAB64201. The human LTBP-3 cDNA can hybridize to the instantly disclosed SEQ ID NO:1, as evidenced by Database GenBank Accession No. AF011407. It would have been obvious of one of ordinary skill in the art at the time of Applicants' invention to test for the binding of the human LTBP-3 polypeptide to calcium or other compounds because YIN suggests that importance of doing so.	reasonable expectation of success, using techniques such as those used by LIN for the recombinant expression of the mouse
ecombinantly because the supply of many eukaryotic proteins which have potential clinical or industrial use is often limited by neir low natural availability; gene cloning and expression in (E. coli, bacteria, yeast, etc.) would provide a more abundant course of the human LTBP-3 polypeptide. Recombinant expression would provide a convenient source of readily purified rotein. The human LTBP-3 polypeptide comprises at least 20 contiguous amino acids of the instantly disclosed SEQ ID 80:2, as evidenced by Database GenBank Accession No. AAB64201. The human LTBP-3 cDNA can hybridize to the instantly disclosed SEQ ID NO:1, as evidenced by Database GenBank Accession No. AF011407. It would have been obvious of one of ordinary skill in the art at the time of Applicants' invention to test for the binding of the human LTBP-3 polypeptide of calcium or other compounds because YIN suggests that importance of doing so.	LTBP-3 polypeptide. One of ordinary skill in the art would be motivated to express the human LTBP-3 polypeptide
neir low natural availability; gene cloning and expression in (E. coli, bacteria, yeast, etc.) would provide a more abundant course of the human LTBP-3 polypeptide. Recombinant expression would provide a convenient source of readily purified rotein. The human LTBP-3 polypeptide comprises at least 20 contiguous amino acids of the instantly disclosed SEQ ID RO:2, as evidenced by Database GenBank Accession No. AAB64201. The human LTBP-3 cDNA can hybridize to the instantly disclosed SEQ ID NO:1, as evidenced by Database GenBank Accession No. AF011407. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to test for the binding of the human LTBP-3 polypeptide to calcium or other compounds because YIN suggests that importance of doing so.	recombinantly because the supply of many eukaryotic proteins which have potential clinical or industrial use is often limited by
rotein. The human LTBP-3 polypeptide comprises at least 20 contiguous amino acids of the instantly disclosed SEQ ID RO:2, as evidenced by Database GenBank Accession No. AAB64201. The human LTBP-3 cDNA can hybridize to the instantly disclosed SEQ ID NO:1, as evidenced by Database GenBank Accession No. AF011407. It would have been obvious of one of ordinary skill in the art at the time of Applicants' invention to test for the binding of the human LTBP-3 polypeptide of calcium or other compounds because YIN suggests that importance of doing so.	their low natural availability; gene cloning and expression in (E. coli, bacteria, yeast, etc.) would provide a more abundant
NO:2, as evidenced by Database GenBank Accession No. AAB64201. The human LTBP-3 cDNA can hybridize to the instantly disclosed SEQ ID NO:1, as evidenced by Database GenBank Accession No. AF011407. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to test for the binding of the human LTBP-3 polypeptide to calcium or other compounds because YIN suggests that importance of doing so.  NEW CITATIONS	source of the human LTBP-3 polypeptide. Recombinant expression would provide a convenient source of readily purified
NO:2, as evidenced by Database GenBank Accession No. AAB64201. The human LTBP-3 cDNA can hybridize to the instantly disclosed SEQ ID NO:1, as evidenced by Database GenBank Accession No. AF011407. It would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to test for the binding of the human LTBP-3 polypeptide to calcium or other compounds because YIN suggests that importance of doing so.  NEW CITATIONS	protein. The human LTBP-3 polypeptide comprises at least 20 contiguous amino acids of the instantly disclosed SEQ ID
o one of ordinary skill in the art at the time of Applicants' invention to test for the binding of the human LTBP-3 polypeptide o calcium or other compounds because YIN suggests that importance of doing so.  NEW CITATIONS	NO:2, as evidenced by Database GenBank Accession No. AAB64201. The human LTBP-3 cDNA can hybridize to the
o one of ordinary skill in the art at the time of Applicants' invention to test for the binding of the human LTBP-3 polypeptide o calcium or other compounds because YIN suggests that importance of doing so.  NEW CITATIONS	instantly disclosed SEQ ID NO:1, as evidenced by Database GenBank Accession No. AF011407. It would have been obvious
calcium or other compounds because YIN suggests that importance of doing so.  NEW CITATIONS	to one of ordinary skill in the art at the time of Applicants' invention to test for the binding of the human LTBP-3 polypeptide
NEW CITATIONS	
NONE	NEW CITATIONS
	NONE

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/19436

	<del> </del>	<del></del>			
	SSIFICATION OF SUBJECT MATTER				
IPC(7) ::CO7K 14/47; C07H 21/04; C12N 1/21, 15/00; C12P 21/00 US CL ::530/350; 536/23.5, 435/7.1, 69.1, 252.3, 320.1					
	According to International Patent Classification (IPC) or to both national classification and IPC				
B. FIEL	DS SEARCHED				
Minimum de	ocumentation searched (classification system followed	i by classification symbols)			
U.S. : :	530/350; 536/23.5, 435 7.1, 69.1, 252.3, 320.1				
Documentat	ion searched other than minimum documentation to the	extent that such documents are included	in the fields searched		
Electronic d	ata base consulted during the international search (na	me of data base and, where practicable,	search terms used)		
WEST, CA					
C. DOC	UMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where app	propriate, of the relevant passages	Relevant to claim No		
Y	YIN et al. Isolation of a novel latent beta-binding protein (LTBP-3). J. Biol 270, No. 17, pages 10147-10160, espec paragraph 1; paragraph bridging page col. 2, last paragraph.	. Chem. 28 April 1995, Vol. cially page 10148, col. 1, full	1-7, 10-12, 14		
Y	GONG et al. Isoforms and splice var factor beta-binding protein in regastroenterology. February 1998, Vol. especially page 352, paragraph bridging 1, full paragraph 1; page 357, paragraph 1;	at hepatic stellate cells. 114, No. 2, pages 352-363, g columns 1-2; page 353, col.	1-7, 10-12, 14		
X Furth	er documents are listed in the continuation of Box C.	See patent family annex			
• Spe	ecial categories of cited documents	*T* ister document published after the inte			
	cument defining the general state of the art which is not considered be of particular relevance	the principle or theory underlying the			
"E" ear	riser document published on or after the international filing date	*X* document of particular relevance, the considered novel or cannot be consider			
çıtı	cument which may throw doubts on priority claim(s) or which is ed to establish the publication date of another citation or other	when the document is taken alone  "Y" document of particular relevance, the	claumed invention cannot be		
*O* do	special reason (as specified)  document referring to an oral disclosure, use, exhibition or other means  on sidered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art				
•P• do	P* document published prior to the international filing date but later than •&• document member of the same patent family the priority date claimed				
Date of the	actual completion of the international search	Date of mailing of the international sea	rch report		
25 JANU	ARY 2000	<b>11</b> FEB 2000			
Commissio Box PCT	mailing address of the ISA US oner of Patents and Trademarks n, D.C. 20231	Authorized atricer Jaurence DAVID S ROMEO	Too		
	40 (703) 305-3230	Telephone No. (703) 308-0196			



International application No. PCT/US99/19436

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
Y	Database GenBank, US National Center for Biotechnology Information, (Bethesda, MD, USA), Accession No. AF011407, MICHEL et al. 'Analysis of the expression pattern of the latent TGF-beta binding protein (LTBP) isoforms in normal and diseased human liver reveals a new splice variant missing part of the proteinase sensitive hinge region', 28 July 1997.	1-7, 10-12, 14
ď	Database GenBank, US National Center for Biotechnology Information, (Bethesda, MD, USA), Accession No. AAB64201, MICHEL et al. 'Analysis of the expression pattern of the latent TGF-beta binding protein (LTBP) isoforms in normal and diseased human liver reveals a new splice variant missing part of the proteinase sensitive hinge region', 28 July 1997.	1-7, 10-12, 14

# INTERNATIONAL SEARCH REPORT



Inemational application No. PCT/US99/19436

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)			
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:			
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:			
Claims Nos.:  because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically			
3 X Claims Nos.: 8-9 because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).			
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)			
This International Searching Authority found multiple inventions in this international application, as follows:			
Please See Extra Sheet.			
1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.			
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.			
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:			
4. X No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-7, 10-12			
Remark on Protest The additional search fees were accompanied by the applicant's protest			
No protest accompanied the payment of additional search fees.			





International application No. PCT/US99/19436

BOX II OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-12, 14, drawn to human LTBP-3 polypeptides and polynucleotides.

Group II, claim(s) 13, 17, drawn to an antibody that binds a human LTBP-3.

Group III, claim(s) 15, 16, 18-20, 25, drawn to a method of administering a human LTBP-3 polypeptide to a patient. Group IV, claim(s) 21, drawn to a method of administering a compound that binds a human LTBP-3 polypeptide to a patient.

Group V, claim(s) 22-24, 26-28, to the extent that they are drawn to a method of modulating the expression of a human LTBP-3 polynucleotide.

Group VI, claim(s) 22-24, 26-28, to the extent that they are drawn to a method of modulating the activity of a human LTBP-3 polynucleotide.

Group VII, claim(s) 29-31, to the extent that they are drawn to a method of manufacturing a medicament comprising a compound that modulates the expression of a human LTBP-3 polynucleotide

Group VIII, claim(s) 29-31, to the extent that they are drawn to a method of manufacturing a medicament comprising a compound that modulates the activity of a human LTBP-3 polynucleotide.

The inventions listed as Groups I-VIII do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons

The special technical feature of the main invention, Group I, is a human LTBP-3 polypeptide. In order for unity of invention to be present the claims must define a special technical feature that makes a contribution over the prior art. However, YIN et al. teach the existence of the human LTBP-3 gene and the isolation of fragments thereof. See the paragraph bridging pages 10157-10158. The human LTBP-3 polypeptide comprises at least 20 contiguous amino acids of SEQ ID NO.2, as recited in claim 1, as evidenced by GenBank database entry accession no. 015107. Accordingly, group I does not fulfill the requirements of unity of invention with respect to a human LTBP-3 polypeptide. Any of groups II-VIII do not share a special technical feature with group I because group I does not have a special technical feature.

Pursuant to 37 CFR 1.475(d), this authority considers that where multiple products and processes are claimed, the first recited product, method of making that product, and method of using that product, together with the first recited of each of the other inventions related thereto, shall constitute the main invention. Further, it considers that any subsequently recited products and/or methods constitute separate groups. Accordingly, groups II-VIII constitute separate groups.

Interress application No.
PCT. 0000/18184

A. CLASSIFICATION OF SUBJECT MATTER  IPC(7) : C07K 14/47; C07H 21/04; C12N 15/63, 1/21; C12P 21/02  US CL : 530/350; 536/ 23.5; 435/320.1, 252.3, 69.1  According to International Patent Classification (IPC) or to both national classification and IPC				
B. FIELDS SEARCHED				
	ocumentation searched (classification system followed	d by classification symbols)		
U.S. : 530/350; 536/ 23.5; 435/320.1, 252.3, 69.1				
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched				
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  Please See Extra Sheet.				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where ap	propriate, of the relevant passages	Relevant to claim No.	
X  Y	CHRETIEN et al. CTX, a Xenopus the molecular family conserved throughout to 1998, Vol. 28, pages 4094-4104, espe	vertebrates. Eur. J. Immunol.	1, 3-5, 8, 12  6, 7, 10	
	acid sequences, and the attached sequer	nce alignment which shows a		
Α	100% identical match to amino acids 2	1-100 of SEQ ID NO:2.	2, 9	
X  Y  A	Sequence Database EST, National Cancer Institute, Cancer Genome Anatomy Project (CGAP), Tumor Gene Index, AN AI478852.  'tm24f09.x1 Soares_NFL_T_GBC_S1 Homo sapiens cDNA clone IMAGE:2157545 3' similar to TR:Q91665 CTX;, mRNA sequence'.  2, 9			
Further documents are listed in the continuation of Box C. See patent family annex.				
'A' do				
to be of particular relevance  'B' sarlier document published on or after the international filing date  "X		X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone		
*L' document which may throw doubts on priority claim(s) or which is zited to establish the publication date of another citation or other special reason (as specified)  *O' document referring to an oral disclosure, use, exhibition or other means		document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art		
	ocument published prior to the international filing date but later than se priority date claimed	'A' document member of the same pater		
	Date of the actual completion of the international search  Date of mailing of the international search report			
31 AUGUST 2000 <b>22 SEP</b> 2000			000	
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231  Authorized officer EILEEN B. O'HARA  (700) 200 0106			L Brings	
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Во	x I O	Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)		
This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:				
1.		Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:		
2.		Claims Nos.: because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:		
3.		Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).		
Bo	x II C	Observations where unity of invention is lacking (Continuation of item 2 of first sheet)		
Th	is Inte	mational Searching Authority found multiple inventions in this international application, as follows:		
	Pk	case See Extra Sheet.		
1.		As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.		
2.		As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.		
3.		As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:		
4.	[X] 1	No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  -10 and 12		
Re	emark	on Protest  The additional scarch fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.		



Internal application No.
PCT/US00/18184

#### **B. FIELDS SEARCHED**

Electronic data bases consulted (Name of data base and where practicable terms used):

Commercial Sequence Databases: GenEmbl, N\_Geneseq\_36, Issued\_Patents\_NA, EST, A\_Geneseq\_36,

Issued\_Patents\_AA, PIR\_64, SwissProt\_38STREMBL\_12

Sequences searched: SEQ ID NOS: 1, 2 and 3

#### BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claim(s) 1-10 and 12, in so far as they are drawn to Tango 244, polynucleotides of SEQ ID NOS: 1 and 3, vector, host cell, method of producing a protein recombinantly and protein of SEQ ID NO:2.

Groups II-V, claim(s) 1-10 and 12, in so far as they are drawn to the next four polynucleotides of distinct cDNA clones and encoded proteins, identified as Tango 246, Tango 275, Tango 300 and human and monkey Mango 245.

Groups VI-X, claims 11 and 15, in so far as they are drawn to antibodies to one of the five proteins listed above. Groups XI-XV, claims 13, 14, 19, 20 and 22, in so far as they are drawn to a method for detecting the presence of in a sample or identifying a compound which binds to or modulates the activity of a polypeptide of one of the five proteins listed above.

Groups XVI-XX, claims 16 and 17, in so far as they are drawn to a method for detecting the nucleic acids of one of the five cDNA clones listed above.

Groups XXI-XXV, claim 18, in so far as it is drawn to a kit comprising a compound of unspecified constitution which selectively binds to a nucleic acid molecule of the five cDNA clones listed above.

Groups XXVI-XXX, claim 21, in so far as it is drawn to a method for modulating the activity of one of the five proteins listed above.

The inventions listed as Groups I-XXX do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Group I corresponds to the first invention wherein the first product is the polynucleotide and the first method of using is the method of making the protein. Note that there is no method of making the polynucleotide. The invention also includes the protein made. Each of groups II-V does not share the same or corresponding special technical feature because each group is drawn to a different polynucleotide and encoded protein, and each of groups VI-XXX does not share the same or corresponding special technical feature because each group is drawn to different compounds or methods of using the five polynucleotides and encoded proteins. This Authority therefore considers that the several inventions do not share a special technical feature within the meaning of PCT Rule 13.2 and thus do not relate to a single general inventive concept within the meaning of PCT Rule 13.1.